

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

see form PCT/ISA/220

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2004/014381

International filing date (day/month/year)  
15.12.2004

Priority date (day/month/year)  
17.12.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D333/54, C07D335/06, A61K31/38, A61P11/00

Applicant  
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1 (a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 10

because:

☒ the said international application, or the said claims Nos. 10 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2004/014381

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-15
	No: Claims	
Inventive step (IS)	Yes: Claims	9
	No: Claims	1-8,10-15
Industrial applicability (IA)	Yes: Claims	1-9,11-15
	No: Claims	

2. Citations and explanations

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

D1: WO 03/024439 A (GLAXO GROUP LIMITED; BOX, PHILIP, CHARLES; COE, DIANE, MARY; LOOKER, B) 27 March 2003 (2003-03-27)

D2: US-A-4 992 474 (SKIDMORE ET AL) 12 February 1991 (1991-02-12)

The present application discloses compounds of the general formula (I) (claims 1-9), a method of prophylaxis or treatment by administering the compounds (I) (claim 10), the compounds (I) for use in therapy (claims 11-12), pharmaceutical formulations thereof (claim 13), the usage thereof for the preparation of a medicament (claim 14) and a process for the preparation thereof (claim 15).

For the assessment of the present claim 10 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The compounds according to the present case are characterized by a terminal benzo-thiophene or thiochromene the heterocyclic part of which is hydrogenated which is also the structural feature distinguishing the compounds (I) according to the present case from

those of D1 and D2, wherein the corresponding terminal ring is a phenyl which may be substituted by monovalent groups (D1, D2) or a (bivalent) alkylendioxy moiety.

The subject-matter of claims 1-15 according to the present case is therefore novel in the sense of Article 33(2) PCT.

As closest prior art can be regarded D2.

The problem of the present application was to provide further phenethanolamine derivatives which are  $\beta_2$ -adrenoreceptor agonists.

It was demonstrated in the description that this problem has been solved by representatives of the compounds (I) in which Ar is (a). There is, however, no evidence that also compounds of formula (I) in which Ar is a group (b), (c) or (d) are a solution to the problem.

The compounds (I) with Ar being a group (a) have to be considered non-obvious for the skilled man, as nothing in D2 gives the skilled person an incentive to substitute the terminal phenyl or alkylendioxyphenyl rest in the compounds disclosed therein by one of the special heterobicyclic rests as present in the compounds (I) of the present case.

An inventive step in the sense of Article 33(3) PCT can thus be acknowledged for the subject-matter of claim 9.

The acknowledgement of an inventive step for claims 1-8 and 10-15 would depend from a.  
the demonstration that also the compounds (I) in which Ar designates (b), (c) or (d) display the alleged pharmacological activities or  
b. restriction to compounds (I) in which Ar designates a group (a)

An inventive step in the sense of Article 33(3) PCT cannot yet be acknowledged for the subject-matter of claims 1-8 and 10-15.

Further objections:

The term "physiologically functional derivative thereof" used in claims 1, 7 and 10-15 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

It is stated in claim 1 that  $R^5$  and  $-NHR^6$  can, optionally, be taken together to form a 5- to 6-membered heterocyclic ring. A skilled reader would understand "heterocyclic ring" as being unsubstituted.

This is in contradiction to the groups (xv) - (xix) according to claim 6 in which  $R^5$  and  $-NHR^6$  form **substituted** 5- to 6-membered heterocyclic rings.

The subject-matter of claim 6 therefore has to be objected under Article 6 PCT.

The structural formula of (I) as displayed in claim 1 and in the description should be corrected (the two rings are not spiro-condensed) (Art. 6 PCT).